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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,440	06/20/2005	Elisabeth Bock	BOCK8	6815

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EXAMINER	
LI, RUIXIANG	
ART UNIT	PAPER NUMBER
1646	
MAIL DATE	DELIVERY MODE
10/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,440	BOCK ET AL.	
	Examiner	Art Unit	
	RUIXIANG LI	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,8,14,15,20,55 and 58-89* is/are pending in the application.

4a) Of the above claim(s) *20, 60, 63-70, 76, 78, 80, 83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,8,14,15,20,58,59,61,62,71-75,77,79,81,82 and 84-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicants' amendment filed upon 07/23/2008 has been entered in full. Claims 1, 4, 5, 8, 14, 15, 20, 55, and 58-89 are pending. Claims 1 (in part), 4, 5, 8, 14, 15, 20, 58, 59, 61, 62, 71-75, 77, 79, 81, 82, 84, 85-89 are currently under consideration. All other claims are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Election/Restriction

The office action mailed on 01/23/2008 requires that Applicants affirm the provisional election of FGFR1. Applicants do no provide a clear statement for such affirmation. However, Applicants' argument on the restriction among fibroblast growth factor receptors implies that Applicants intend to affirm the provisional election of FGFR1.

In the reply filed on 07/23/2008, Applicants continue to traverse the restrictions among fibroblast growth factor receptors and binding polypeptides. Applicants' argument has been considered, but is not deemed persuasive for the following reasons.

REQUIREMENT FOR UNITY OF INVENTION

As provided in 37 CFR 1.475(a), a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in a national stage application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special

technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim. See 37 CFR 1.475(e).

When Claims Are Directed to Multiple Categories of Inventions

As provided in 37 CFR 1.475(b), a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

(1)A product and a process specially adapted for the manufacture of said product; or

(2)A product and process of use of said product; or

(3)A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4)A process and an apparatus or means specifically designed for carrying out the said process; or

(5)A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

Otherwise, unity of invention might not be present. See 37 CFR 1.475(c).

Chemical Compound Alternatives of Markush Group Are Not of a Similar Nature

Where a single claim defines alternatives of a Markush group, the requirement of a technical interrelationship and the same or corresponding special technical features as defined in Rule 13.2, is considered met when the alternatives are of a similar nature. When the Markush grouping is for alternatives of chemical compounds, the alternatives are regarded as being of a similar nature where the following criteria are fulfilled:

(A) all alternatives have a common property or activity; AND

(B)(1) a common structure is present, that is, a significant structural element is shared by all of the alternatives; OR

(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

The phrase "significant structural element is shared by all of the alternatives" refers to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity.

The phrase "recognized class of chemical compounds" means that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention, i.e. each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

(i). Newly amended claim 1 (in part) and newly submitted claims 60, 63-70, 76, 78, 80, and 83 directed to a method of modulating the interaction between a functional cell-surface fibroblast growth factor receptor and a polypeptide comprising SEQ ID NO: 9, said method comprising providing (II) a multimer comprising a plurality of monomers, each monomer being independently a peptide of (I). The invention that lacks unity with the invention originally claimed for the following reasons:

The chemical compounds of (I) and (II) recited in claim 1 are not regarded as being of similar nature because: (1) all the alternatives do not share a common structure and (2) the alternatives do not all belong to a recognized class of chemical compounds. Compounds of (I) encompass a peptide of 6-16 amino acid residues and comprises (a) a sequence which is at least 80% identical to SEQ ID NO: 9, or (b) a fragment, at least 6 a.a. in length, of (a), whereas compounds of (II) are directed to a multimer comprising a plurality of monomers, each monomer being independently a peptide of (I). For example, a multimer comprising SEQ ID NO: 132 does not share a common structure

with SEQ ID NO: 9 and they do not appear to belong to a recognized class of chemical compounds.

It is further noted that the prior art teach the instantly claimed methods. Even if the inventions of these groups require the technical feature of a method of modulating the interaction of FGFR and a binding polypeptide comprising SEQ ID NO: 9, this technical feature is not a special technical feature as it does not make a contribution over the prior art in view of Skladchikova et al. (*J Neurosci Res.* 57(2):207-218, 1999).

Skladchikova et al. teach neural cell adhesion molecule (NCAM) comprising two fibronectin type-III modules (page 208, left column, lines 8-9), which have been demonstrated to induce neurite outgrowth and cell adhesion (page 208, left column, lines 31-32). Skladchikova et al. teach that NCAM interacts with FGFR through CHD located in the second Ig module of the FGFR and a site for recognition of FGFR-CHD is located in the first Fn-III module of NCAM, which necessarily comprises the amino acid sequence of SEQ ID NO: 9.

Skladchikova et al. teach modulation of NCAM-FGFR interaction with a fragment of FGFR (the FGFR-CAM homology domain or CHD), an anti-FGFR antibody, an anti-NCAM antibody (an antibody against the NCAM-Fn-III 1-2 modules), as well as ATP in rat hippocampal neuronal cultures that necessarily express FGFR1 (page 212, last paragraph of left column to the 1st paragraph of right column; Fig. 10). FGFR antibodies, CHD, and NCAM antibodies all abrogated ATP-stimulated neurite outgrowth (page 212, the 1st paragraph of right column; Fig. 10).

Skladchikova et al. do not teach modulation of NCAM-FGFR interaction with a peptide of 6-16 amino acid residues that comprises a sequence which is at least 80% identical to SEQ ID NO: 9 or a fragment thereof at least 6 a.a. in length. However, it would have been obvious to one having ordinary skill in the art at the time the invention was made, as an alternative approach, to modulate NCAM-FGFR interaction with a peptide derived from the first Fn-III module of NCAM with a reasonable expectation of success. One would have been motivated to do so because the first Fn-III module of NCAM is the site for recognition of FGFR-CHD as taught by Skladchikova et al.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, newly amended claim 1 (in part) and newly submitted claims 60, 63-70, 76, 78, 80, and 83 are withdrawn from consideration as being directed to a nonelected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

(ii). Restriction to FGFR1 is maintained

The chemical compounds of FGF receptors as listed in claim 4 are not regarded as being of similar nature because all of the alternatives do not share a common property or activity. Activation of FGF receptors by different FGF leads to diverse biological response in various cell types (see, e.g., Stauber et al. PNAS 97:49-54, 2000; Powers et al. Endocrine-Related Cancer 7:165-197, 2000).

It is further noted that the prior art teach the instantly claimed methods, as noted above.

(iii). Restriction to SEQ ID NO: 9 is maintained.

Likewise, the recited polypeptides set forth in SEQ ID NOS: 9, 75, 78-85, 87, 89-91, 93-95, and 132 are not regarded as being of similar nature because: (1) all the alternatives do not share a common structure and (2) the alternatives do not all belong to a recognized class of chemical compounds. For example, SEQ ID NO: 9 and SEQ ID NO: 132 do not share a common structure and they do not appear to belong to a recognized class of chemical compounds. Moreover, the polypeptides set forth in SEQ ID NOS: 9, 75, 78-85, 87, 89-91, 93-95, and 132 do not appear to share a common property or activity. For example, they do not appear to bind the same FGF receptors and producing same biological responses.

It is further noted that the prior art teach the instantly claimed methods, as noted above.

(iv). Applicants' request for rejoinder

Claim 20 will be rejoined. Claim 55 will not be rejoined because the elected Invention Group I and claim 55 of Invention Group V (see Restriction/Election Requirement mailed on 09/13/2007) are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept.

It is further noted that the prior art teach the instantly claimed method of claim 1, as noted above.

Finally, the examiner clarifies that since all the cell adhesion molecules listed in the claim 8 comprises SEQ ID NO: 9, they will be examined together.

The requirement is still deemed proper and is therefore made FINAL.

Withdrawn Objections and/or Rejections

The rejection of claims 1, 4, 5, 8, 14, 15, 17, and 18 under 35 U.S.C. 112, second paragraph is withdrawn in view of amended claims.

The rejection of claims 1, 8, 14, 15, 17, and 18 under 35 U.S.C. 112, first paragraph, for written description is withdrawn in view of amended claim 1 and canceled claims 17 and 18.

The rejection of claims 1, 4, 5, 8, 14, 15, 17, and 18 are rejected under 35 U.S.C.§ 102(b) as being anticipated by Skladchikova et al. (*J Neurosci Res.* 57(2):207-218, 1999) is withdrawn in view of amended claims.

The objection to drawings is withdrawn in view of amended specification, which identifies the amino acid sequences present in Figs. 6, 8, and 10 in the legends of the figures.

Claim Rejections Under 35 U.S.C. §112, 1st Paragraph

(i). The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(ii). Claims 1, 4, 5, 8, 14, 15, 20, 58, 59, 61, 62, 71-75, 77, 79, 81, 82, 84, and 85-89 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was

not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

The elected invention of claim 1 is drawn to a method of modulating the interaction between a FGFR1 and a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 9 with a compound capable of interacting with the receptor at the binding site of the receptor for the polypeptide, wherein said compound is a peptide of 6-16 amino acid residues and comprises (a) a sequence which is at least 80% identical to SEQ ID NO: 9, or (b) a fragment, at least 6 a.a. in length of (a). All other claims depend from claim 1. Claim 1, as written, does not require that a homologue of SEQ ID NO: 9 or a fragment possess any particular structure nor a conserved binding domain.

The specification discloses that a protein consisting of the NCAM F3 modules 1, 2 binds to an immobilized protein comprising the FGFR modules 2, 3 (page 66, the 2nd

paragraph). The specification further discloses that the EF loop peptide (SEQ ID NO: 9) induces neuritogenesis (page 71, last paragraph of the specification). However, there is no description of the conserved regions in SEQ ID NO: 9 that are critical for the binding to FGFR1. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to the binding activity. Furthermore, Skladchikova et al. teach modulation of NCAM-FGFR interaction with a fragment of FGFR (the FGFR-CAM homology domain or CHD), an anti-FGFR antibody, an anti-NCAM antibody (an antibody against the NCAM-Fn-III 1-2 modules), as well as ATP in hippocampal neuronal cultures that necessarily express FGFR1 (page 212, last paragraph of left column to the 1st paragraph of right column; Fig. 10). FGFR antibodies, CHD, and NCAM antibodies all abrogated ATP-stimulated neurite outgrowth (page 212, the 1st paragraph of right column; Fig. 10). However, the prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed homologues of SEQ ID NO: 9 and fragments recited in claim 1.

Due to the breadth of the encompassed genus of homologues of SEQ ID NO: 9 and fragments recited in claim 1 and lack of the definitive structural features of the encompassed genus, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the encompassed genus of homologues of SEQ ID NO: 9 and fragments recited in claim 1 and thus the instantly claimed method.

Claim Rejections under 35 USC § 103

(i). The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(ii). Claims 1, 4, 5, 8, 14, 15, 20, 58, 59, 61, 62, 71-75, 77, 79, 81, 82, 84, 85-89 are rejected under 35 U.S.C.§ 103(a) as being unpatentable over Skladchikova et al. (*J Neurosci Res.* 57(2):207-218, 1999).

Skladchikova et al. teach neural cell adhesion molecule (NCAM) comprising two fibronectin type-III modules (page 208, left column, lines 8-9), which have been demonstrated to induce neurite outgrowth and cell adhesion (page 208, left column, lines 31-32). Skladchikova et al. teach that NCAM interacts with FGFR through CHD located in the second Ig module of the FGFR and a site for recognition of FGFR-CHD is located in the first Fn-III module of NCAM, which necessarily comprises the amino acid sequence of SEQ ID NO: 9.

Skladchikova et al. teach modulation of NCAM-FGFR interaction with a fragment of FGFR (the FGFR-CAM homology domain or CHD), an anti-FGFR antibody, an anti-NCAM antibody (an antibody against the NCAM-Fn-III 1-2 modules), as well as ATP in rat hippocampal neuronal cultures that necessarily express FGFR1 (page 212, last paragraph of left column to the 1st paragraph of right column; Fig. 10). FGFR antibodies,

CHD, and NCAM antibodies all abrogated ATP-stimulated neurite outgrowth (page 212, the 1st paragraph of right column; Fig. 10).

Skladchikova et al. do not teach modulation of NCAM-FGFR interaction with a peptide of 6-16 amino acid residues that comprises a sequence which is at least 80% identical to SEQ ID NO: 9 or a fragment thereof at least 6 a.a. in length. However, it would have been obvious to one having ordinary skill in the art at the time the invention was made, as an alternative approach, to modulate NCAM-FGFR (such as FGFR1 from rat, human or mouse) interaction with a peptide derived from the first Fn-III module of NCAM with a reasonable expectation of success. One would have been motivated to do so because the first Fn-III module of NCAM is the site for recognition of FGFR-CHD as taught by Skladchikova et al.

Comment [R1]:

Claim Objections—Minor Informalities

Claims 1, 4, 8, 14, 15, 20, 58, 59, 61, 62, 71-75, 77, 79, 81, 82, 84-87 are objected to because recite non-elected fibroblast growth factor receptors, binding polypeptides, or multimers.

Claim 1 is objected to because of a typographic error in line 11: "comprises (a) comprising".

Appropriate correction is required.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/
Primary Examiner, Art Unit 1646

October 10, 2008